Allergy Abstracts

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From the Allergy Division of
The Jewish Hospital of Brooklyn

Volume 23, Number 1 January, 1958

Asthma and Hay Fever

The Treatment of the Acute Asthmatic Attack With an Oral Alcohol-Water Solution of Theophylline (Elixophyllin). Schluger, J., McGinn, J. T., and Burbank, B.: Am. J. M. Sc. **234**: 28, 1957.

Fifty unselected asthma patients who came to the emergency room of a large hospital for relief of an acute attack were treated with Elixophyllin. The study included 24 males and 26 females whose ages ranged from 17 to 67 years. Elixophyllin contains 20 per cent ethyl alcohol and 80 mg. of theophylline in each 15 ml. Each patient was given from 69 to 75 ml. of the alcohol-water solution of theophylline in a single dose, and the immediate effects of the medication were studied. If the patient was not relieved within 30 minutes, Adrenaline or intravenous aminophylline was administered to interrupt the attack. Of the 50 patients treated, 37 (74 per cent) obtained complete relief from the oral medication. Five patients (10 per cent) obtained partial relief, but further treatment with either Adrenalin or aminophylline was necessary. Eight patients (16 per cent) obtained no relief and 4 of these

also failed to respond to either intravenous aminophylline or Adrenalin and had to be hospitalized. One of the 50 patients complained of abdominal pain and vomited following the oral medication, but there was a minimum of gastrointestinal symptoms noted in the other patients. R. W.

The Limited Use of Chlorpromazine in Bronchial Asthma. Michelson, A. L., and Lowell, F. C.: Am. J. M. Sc. **234**: 31, 1957.

In order to evaluate the possible beneficial effects of chlorpromazine in relieving asthma, the authors studied its action on 7 asthmatic patients and 7 normal controls. Each patient was given saline intravenously for 15 to 30 minutes, followed by an infusion containing 15 to 25 mg. of chlorpromazine dissolved in 250 ml. of fluid. Patients were not informed when the chlorpromazine was substituted for the saline. The solution containing the chlorpromazine was given at 100 drops a minute, so that the administration took about 15 to 20 minutes. The infusions were all given without incident. Most of the patients noticed a marked sedative effect from the medication. Both the asthmatic patients and the control subjects showed an increase in pulse rate and a drop in blood pressure. Respiratory changes were studied by closed-system spirometry. There was an increase in respiratory rate in the majority of both groups, and the tidal volume dropped in 6 out of 7 patients in both groups. Total vital capacity was essentially unchanged in each group. Electrocardiographic studies made during the infusion showed slight flattening of the T waves in the precordial leads in 2 subjects in each group. R. W.

Development and Course of Asthma in Children. Dees, S. C.: A. M. A. Am. J. Dis. Child. **93**: 228, 1957.

The histories of 239 children with atopic or allergic eczema who were seen at the Duke Hospital Allergy Clinic from 1930 to 1945 are reviewed. Seventy patients, or 30 per cent, subsequently developed asthma. After the onset of their eczema, about one-eighth of these children developed asthma within 6 months to 1 year, about one-third within 1 to 3 years, and about one-half within 3 to 15 years. There appeared to be a tendency for asthma to develop earlier in the children whose eczema began prior to 3 months of age.

Of 269 asthmatic children seen in the first 5 years of the Duke Pediatric Allergy Clinic, 233 cases were available for review. These patients had been treated by active immunization, avoidance of allergens, and dietary restriction. One hundred four, or 44 per cent, did well after 2 years of treatment. Eighty-six patients, or 36 per cent, were improved but still had moderate difficulty, and 46, or 20 per cent, were unimproved. Since 6,737 patients died of asthma in the United States during 1953, and in view of the fact that asthma is to a great extent a preventable disease, the author stresses the importance of treating allergic rhinitis and eczema, the important pediatric precursors of asthma. R. W.

Study of the Role of Antigen Dosage in the Treatment of Pollenosis and Pollen Asthma. Johnstone, D. E.: A. M. A. Am. J. Dis. Child. **94**: 1, 1957.

A series of 175 children with ragweed hay fever or asthma were treated by one of four dosage programs in an attempt to evaluate the importance of total dosage in the effectiveness of the therapeutic results. Each child was thoroughly studied in the pediatric clinic before referral to the allergy clinic, where a complete allergy work-up was done. Four dosage programs were outlined and the children were placed in one of the groups in rotation. In the

first group dosage was increased gradually toward the maximum that could be comfortably tolerated by the patient. In most instances, this amounted to about 0.5 ml. of a 1:200 or 1:500 dilution of ragweed in Coca's solution, which was equivalent to 1,250 to 2,500 Noon units. The second group comprised those youngsters who were given moderate doses of antigen. The top dose in this group was 0.5 ml. of a 1:5,000 dilution (100 Noon units). In the third group, the top dose never exceeded 0.5 ml. of the 1:10 million dilution (0.5 Noon units). The fourth group was given weekly injections of buffered saline. The study was done in Rochester, New York, during the 1956 pollen season and it was observed that the counts that year were lower than in 1955.

There was a marked improvement in Groups 1 and 2, who had received the larger doses of ragweed. There was no improvement in the children who had received extremely small quantities of ragweed or in the control group. In the asthmatic children receiving the highest dosage, 68 per cent had no asthma during this pollen season and no new cases of pollen asthma developed. Results in the group treated with the more moderate doses were almost as good. In the group which received the 1:10 million dilution, only 19 per cent of the pollen asthma children were free of asthma as a result of treatment, and 60 per cent of the children in this group developed pollen asthma for the first time. In the control group only 7 per cent with a history of pollen asthma lost their asthma as a result of treatment, while 42 per cent developed asthma for the first time. Since minute doses of pollen extract were ineffective in the treatment of ragweed pollinosis, it is concluded that adequate total dosage is a significant factor in the patient's response to treatment. R. W.

Dermatology

Atopic Dermatitis Due to Inhalants. Diamond, H. E.: New York J. Med. **57**: 754, 1957.

The importance of inhalant allergens as causative factors in atopic dermatitis has been stressed by many investigators. Among 23 cases of atopic dermatitis previously reported, the author found that, in 9 cases, dust, ragweed, other pollens, and molds were contributing etiologic factors. He also noted the frequent association of atopic dermatitis with respiratory allergy. In the present study of 526 cases of allergy observed over a period of 6 years, there were 427 cases with respiratory symptoms alone. There were 63 cases with respiratory allergy and dermatitis and 36 cases with dermatitis alone. The incidence of atopic dermatitis in patients with respiratory allergy therefore was 13 per cent. Among 36 patients who developed dermatitis before the age of 5 years, 27 also had respiratory symptoms; in 22 of these, the dermatitis preceded the respiratory symptoms. In marked contrast to the latter group, there were 36 cases in which both dermatitis and respiratory symptoms began after the age of 5 years, and in 26 of these the respiratory symptoms preceded the dermatitis. It was also found that a blood eosinophilia was present in 50 per cent of the cases of dermatitis associated with respiratory symptoms, whereas blood eosinophilia was noted in only 13 per cent of cases with dermatitis alone.

In atopic dermatitis due to inhalants the most common offenders were house dust, ragweed, timothy, and tree pollens, and sheep's wool, in that order of frequency. Molds, kapok, and animal danders were less frequent offenders.

Hyposensitization therapy with inhalant extracts in the management of atopic dermatitis yields excellent results. However, extreme caution must be exercised in dosage since exacerbations are common. The author begins therapy with 0.1 ml. of a 1:5,000 or a 1:50,000 dilution of house dust extract

and with 0.1 ml. of pollen extract containing 0.00001 mg. N. per milliliter. He believes that these doses are optimal even in cases where bronchial asthma and hay fever are associated with the dermatitis. When an intercurrent respiratory infection occurs, treatment is stopped or the dosage is diminished temporarily until the infection subsides. Two detailed case histories illustrating the method of therapy are included in this report. M. A.

Studies on Atopic Dermatitis. II. Melanin Distribution and Dopa Oxidase Reaction. Rappaport, B. Z.: A. M. A. Arch. Path. **61**: 318, 1956.

Studies were made to compare the distribution of melanin in the skin from areas of atopic dermatitis and from areas of normal skin. The material consisted of biopsy specimens obtained from 13 patients, of whom 8 were females varying in age from 26 to 40 and 5 were males varying from 21 to 26 years. Eight patients were white and 5 were Negroes. The specimens were taken from sites of typical atopic dermatitis and from normal areas which had not been exposed to sunlight during the previous 6 months. In areas of acute dermatitis with marked edema, melanin had disappeared from the epidermal cells. The diminution of melanin granules within the epidermal cells seemed to be related to the degree of edema in the epidermis. In a patient with subacute or chronic lesions of atopic dermatitis, where epidermal edema was less marked, a moderate number of pigment granules were present within the basal cells of the epidermis as well as outside the cells in the intercellular spaces. Where no edema was present, as in healed atopic dermatitis, there was abundant pigment within the epidermal cells similar to that observed in normal skin. It is suggested that the edema results in a break of contact between basal cells and dendritic processes of the melanocytes interfering with inoculation of pigment into the epidermal cells. As a result, melanin flows directly into the dermis and is ingested by chromatophores. Since, in the epidermis, only the melanocytes stain with dopa solution, this reaction affords a means of studying melanin distribution. The intensity of the dopa reaction was related to the acuteness of the lesion, being greater in the acute than in the subacute lesions, less in "healed" areas of skin, and least in normal skin. J. S.

Studies on Atopic Dermatitis. III. The Effect of Corticotropin, Cortisone, and Hydrocortisone on Storage of Melanin in Basal Cells and on Dopa Oxidase Reaction. Rappaport, B. Z.: A. M. A. Arch. Path. **61**: 395, 1956.

It had previously been shown that in atopic dermatitis the basal cells of the epidermis in areas of active lesions lose their stored melanin and that the pigment granules accumulate in the intercellular spaces. The melanocytes in these areas reacted more strongly with dopa than those in uninvolved skin. As the atopic dermatitis improved, melanin tended to return to the basal cells of the epidermis and the melanocytes reacted less intensely with dopa solution.

Because of the favorable therapeutic action of hormones on atopic dermatitis, the effect of corticotropin and corticoid hormones on melanin storage in basal cells and on the dopa oxidase reaction was studied. Skin biopsies were obtained from 7 women, ranging in age from 26 to 40, and 5 men from 21 to 26 years of age. Seven specimens were from white patients and 5 were from Negro patients. Specimens of skin were studied from involved and uninvolved areas before and after courses of treatment with corticotropin, cortisone, and hydrocortisone. The uninvolved areas of skin had not been exposed to sunlight for at least 6 months. Following treatment, biopsy specimens from areas of dermatitis showed reduction in intercellular edema and restoration of melanin

within the basal cells of the epidermis. In specimens from uninvolved skin areas, melanin distribution was not altered. Similarly, the intensity of the dopa reaction tended to be reduced in areas of dermatitis. This effect was also seen in specimens from uninvolved skin following hormonal treatment. Explanations for this latter phenomenon are offered. J. S.

Chlorpromazine Dermatitis in Nurses. Seville, R. H.: Brit. J. Dermat. **68**: 332, 1956.

Contact dermatitis developed in 11 nurses and one pharmacist following repeated handling of chlorpromazine. Sensitivity in 5 of the patients started with redness, swelling, and occasional weeping of the skin of the face, especially around the eyes and mouth. In the remaining patients, the rash occurred in the clefts or on the sides of the fingers. After the acute reaction had subsided, a dry scaling dermatitis remained which cleared up completely when the patient remained away from the hospital and avoided exposure to sunlight. Recovery followed the use of a rigid "no touch technique." M. C.

Studies of the Mechanism of Allergic Eczematous Contact Dermatitis. 1. Findings on Human Skin With Radioactive Bichloride of Mercury. Witten, V. H., Grayson, L. D., and Birnbaum, V. H.: J. Invest. Dermat. **28**: 339, 1957.

The pathogenesis of allergic eczematous contact dermatitis in man was studied by the use of radioactive bichloride of mercury ($HgCl_2$) in which the mercury was the tagged allergen. Uniform patch tests with a 1:1,000 dilution of a 0.5 per cent aqueous solution of $HgCl_2$ were carried out in normal persons and in individuals with known eczematous allergic sensitivity to this compound. The solution of radioactive bichloride of mercury was applied to selected areas on the lower back. The patches were removed after 48 hours and the sites excised. The biopsy specimens were prepared by one or more specific methods. In each instance, the cut tissue sections were placed on nuclear track plates for 10 to 21 days to produce autoradiograms which could be read under the microscope.

No differences in the routes of penetration, sites of deposition, and localization of radioactively labeled allergen were shown in the skins of known specifically allergic or nonallergic persons. In both groups of subjects, autoradiograms regularly demonstrated the radioactive mercury to be on the surface and within the epidermis, usually in the hair follicles and occasionally in sweat ducts. There was no evidence of the spread of radioactivity even one inch away from the patch test site. The authors pointed out that there may be quantitative differences in the radioactive mercury deposits in the allergic as compared to the nonallergic subjects, but the technique employed in these experiments would not permit such a fine differentiation. T. Chao.

Transfer of Allergic Contact-Type Delayed Sensitivity in Man. Epstein, W. L., and Kligman, A. M.: J. Invest. Dermat. **28**: 29, 1957.

Three contact allergens, pentadecyl catechol (P.D.C.), 2, 4-dinitrochlorobenzene (D.N.C.B.), and paranitrosodimethylaniline (N.D.M.A.) were used to study the transfer of contact sensitivity in man.

Patch tests were performed by placing the test substance in acetone in a round cup, 2.9 cm. in diameter, on the skin of the forearm. A stream of air evaporated the acetone, leaving the test material deposited as fine crystals on

the skin. The selected donors were highly and naturally sensitive to P.D.C., which is present in members of the genus Rhus. They had been artificially sensitized to N.D.M.A. and D.N.C.B. P.D.C. donors constituted a separate series, and another series served for the other two allergens. Recipients of P.D.C. transfers showed no previous sensitivity to a 1:100 patch test. Recipients of cells from D.N.C.B. and N.D.M.A. donors were not initially tested because of the danger of active sensitization from the patch.

Transfer materials were obtained from bullae induced by the allergen, by cantharidin, or by a combination of both. In addition, leukocytes were obtained from whole blood by a special technique. Total numbers of lymphocytes in each preparation were accurately determined. Each recipient received several deep intracutaneous injections of either the leukocyte suspension from blood or the uncentrifuged blister fluid. Challenging patches with 1:100 P.D.C. and 1:1,000 D.N.C.B. and N.D.M.A. were applied to both the injected sites and the normal skin. Sensitization was invariably general. Patch test reactions in P.D.C. recipients were followed over a period of many months, but those in N.D.M.A. and D.N.C.B. recipients were challenged only once or twice during the first six days because of the danger of active sensitization from the patch tests.

With preparations containing adequate numbers of cells, P.D.C. sensitivity was readily transferred in 17 out of 19 cases with blister fluid from all three sources as well as with peripheral blood leukocytes. N.D.M.A. and D.N.C.B. sensitivity could be transferred in 5 out of 13 cases, but only by peripheral blood lymphocytes in numbers greater than 170 million. It was also possible to transfer sensitivity with cell-free blister fluid, suggesting the presence of free antibody. Difficulty in transferring P.D.C. sensitivity to children indicated that previous exposure, without the development of clinical sensitivity, might be a prerequisite. It appeared that the transfer of contact-type delayed sensitivity could be demonstrated in man when the donor was highly sensitive and when the number of cells in the transfer material was sufficient. Successful transfer also seemed to depend upon the nature of the allergen and the individual pattern of response of the recipient. H. STRYKER.

Miscellaneous Allergies

Penicillinase in the Treatment of Penicillin Reactions. Minno, A. M., and Davis, G. M.: J. A. M. A. **165**: 222, 1957.

Penicillinase was used in the treatment of 32 patients who had developed delayed allergic reactions to either procaine or benzathine penicillin. The reactions treated consisted of generalized urticaria, pruritus, fever, arthralgia and, in one case, a hemorrhagic eruption. The penicillinase was usually given intramuscularly in doses of 1 million units in 2 c.c. of sterile distilled water. Within 24 hours, 15 patients became asymptomatic. Five others became asymptomatic within 48 hours. Symptoms disappeared in the remaining 12 patients after 4 to 6 days. Two patients received the penicillinase intravenously. In one, urticaria disappeared within 6 hours and there were no further complaints. The other patient developed a severe shaking chill with high temperature, nausea, and slight cyanosis, requiring epinephrine and steroids for relief. One patient with serum sickness, who had responded favorably to a single injection of penicillinase, had a recurrence one week later and again obtained relief following a second injection of penicillinase. No toxic effects were encountered with the intramuscular use of penicillinase, although local pain and tenderness at the site of injection usually occurred. While it appeared that penicillinase is therapeutically effective in penicillin

reactions, its effects were difficult to evaluate because the severity of the penicillin reactions was variable and because some patients with moderately severe symptoms recovered completely within 24 hours after treatment with a placebo. M. C.

Fatal Bromsulphalein Reaction. Walker, H. C., Jr., and Koszalka, M. F.: Ann. Int. Med. **47**: 362, 1957.

A 58-year-old laborer received 9.5 c.c. of a 5 per cent solution of bromsulphalein intravenously. It was given slowly, although the exact length of time was not determined. There were no local or systemic symptoms immediately following the injection. Several minutes later the patient complained of a frontal headache and became cold and clammy. His radial pulse became imperceptible and he died before any therapy could be given. Post-mortem examination failed to disclose any significant pathologic findings. The patient had previously received bromsulphalein about 3 months prior to the present administration. The authors suggest that the intravenous injection of the dye be given slowly, by the clock, over a period of five minutes and that a skin test be performed in patients with a positive history of allergy. M. C.

Studies on the Immunochemical Basis of Allergic Reactions to Dextrin in Man. Kabat, E. A., Turino, G. M., Tarrow, A. B., and Maurer, P. H.: J. Clin. Invest. **36**: 1160, 1957.

Dextran, which is used to treat shock as a plasma volume expander, is also encountered as a contaminant of commercial sugar and is produced by certain organisms in the gastrointestinal tract. It may react with various rabbit and horse antipneumococcal sera. Precipitable antibody and immediate wheal type reactions to dextran may occur in persons not previously immunized with it. Various preparations of dextran were employed in this study on 207 volunteer subjects. Dextrans of high molecular weight or of great structural complexity produced a high incidence of positive skin reactions and systemic allergic reactions upon infusion. There was a high correlation between initial skin sensitivity to native dextran and systemic allergic reactions, but a number of exceptions were found. Systemic reactions included flushes, headache, angioedema, urticaria, rhinitis, lacrimation, asthma, hypotension, syncope, nausea and vomiting, and swelling of the extremities. There was often a flare-up of previous skin test sites. E. K.

Polyarteritis Nodosa. Report of a Case With Proof of Drug Allergy. McLetchie, N. G. B., MacDonald, R. M., and Cutts, J. H.: Canad. M. A. J. **76**: 213, 1957.

A 45-year-old white man developed muscle pains, frequency, nocturia, headache, fever, and swelling of the left forearm 48 hours following discharge from the hospital where he had been treated for a severe bout of tonsillitis. He had received penicillin and streptomycin intramuscularly and sulfonamides orally for 2 days for relief of the tonsillitis. He was readmitted to the hospital on the twelfth day following his first admission with a temperature of 103° F., two painful nodules on the flexor and dorsal surfaces of the left forearm, and marked tenderness over several tendons in both legs. He was given a course of chloramphenicol for several days without any improvement. All the laboratory studies were essentially negative. He developed red, indurated, tender nodules on his ankle, forearm, and over the temporal artery. After biopsy of one of these nodules, a provisional diagnosis of allergic vasculitis

was made. On cortisone therapy, symptoms improve rapidly and the patient was discharged after 4 weeks of hormone therapy. He was kept on a maintenance dosage of 50 mg. daily and made an uneventful recovery. It was suspected that one of the drugs administered had produced the vascular reaction. Blood was drawn for passive transfer studies on the sixty-third day of the patient's illness, when he had been on cortisone therapy for 43 days. A volunteer was sensitized in five different sites with 1 ml. of the patient's serum and challenged 24 hours later with Dicrysticin (penicillin and streptomycin) and with sulfathiazole. Some of the sites were left untested as controls. Six hours after testing by the intracutaneous or scratch methods, the sites tested with Dicrysticin became intensely itchy and red. By the following morning firm subcutaneous lumps had formed at these sites. One lump was removed and on section showed a generalized vasculitis in the dermis and underlying panniculus. All the small vessels were obscured by lymphocytes and the small peripheral vessels showed marked dilatation and swelling of the endothelial cells. Passive transfer tests with penicillin G and dihydrostreptomycin sulfate resulted in a mild itching reaction on the sites challenged with penicillin. A third volunteer was sensitized with the patient's serum plus a suspension of cells from the buffy coat of the patient's blood. When the sites were challenged 24 hours later with various antigens, a definite subcutaneous lump approximately 1 cm. in diameter with slight erythema occurred in the site tested with penicillin G. The area was excised and paraffin sections showed a reaction similar to that observed with Dicrysticin. R. W.

A Case of Fatal Shock Following Oral Penicillin. Mason, L. H.: Canad. M. A. J. **76**: 958, 1957.

The author reports the case of a 2-year-old child who died following the administration of V-Cillin pediatric drops for tonsillitis and an acute respiratory infection. She had had a similar respiratory infection one year previously, at which time she had been treated with 100,000 unit doses of oral Bicillin without incident. The family history was negative for allergy. Within 30 minutes after the first dose of V-Cillin the child became wheezy and dyspneic. Her symptoms became progressively worse for the next half-hour and she was rushed to the hospital. She was moribund by the time she reached there. In spite of intubation, oxygen by positive pressure, and intravenous Adrenalin, she died within a few minutes after admission. Permission for a post-mortem examination could not be obtained. R. W.

Aspirin Allergy. Walton, C. H. A., and Randle, D. L.: Canad. M. A. J. **76**: 1016, 1957.

The authors reviewed 83 cases of aspirin sensitivity which they had observed among 4,761 allergic patients over a 10-year period. The incidence of aspirin sensitivity in the entire series was 1.74 per cent. None of these patients were being treated primarily because of their aspirin sensitivity.

Of the 83 patients with aspirin sensitivity, 78 had asthma, 55 had allergic rhinitis, 33 had nasal polyps, 18 had urticaria, 3 had migraine, 8 had atopic dermatitis, and 13 had some other form of drug sensitivity. Most of the asthmatic patients sensitive to aspirin reacted with asthma following ingestion of the drug, but 9 with very mild asthma developed either hives or rhinitis following its use. Approximately one-third of the aspirin-sensitive asthmatic patients were considered to have only mild asthma, but 12 out of 29 of these patients developed alarmingly severe asthma following the use of aspirin.

During the 10-year study period, 10 patients in the series died but not as a result of aspirin sensitivity. Actuarial analysis showed this mortality incidence to be approximately 6 times the expected normal and about 4 times the expected incidence in the asthmatic population.

About one-half the patients developed their aspirin sensitivity between the ages of 16 and 40 years and the remainder at a later age. There were no children in the series. Aspirin sensitivity was about twice as common among women as among men. Most of the patients gave a positive history of allergy. An eosinophilia of 4 per cent or more was encountered in at least 60 per cent of the patients. Fifty-nine of the 75 patients in the series who were tested showed positive skin reactions to some allergen. Of these 42 reacted to pollens, 33 to animal danders, and 54 to dust. R. W.

Lupus Erythematosus Disseminatus After Administration of Mesantoin. Report of Two Cases. Lindqvist, T.: Acta med. scandinav. **158**: 131, 1957.

Two cases are reported in which the typical picture of lupus erythematosus disseminatus appeared following the administration of Mesantoin for epilepsy. In one girl, the onset of lupus was noted about one year after the initiation of Mesantoin therapy. This patient also received Epanutin. Symptoms abated when both these drugs were discontinued and returned on resumption of the medications. The patient was hospitalized with severe disability. On treatment with ACTH and the cessation of epileptic medication, her symptoms gradually cleared. No L.E. cells were found at any time. In a second girl, a frank clinical picture of lupus was noted about 13 months after the onset of Mesantoin therapy. This patient was also receiving phenobarbital and Epanutin and had not been well since about one month after Mesantoin was added to Epanutin therapy. Mesantoin was stopped in February, 1954, but the condition grew worse, necessitating hospitalization of the patient in March, 1954. Treatment with ACTH was started and recovery followed. There has been no recurrence. Typical L.E. cells were found in this case. E. K.

Papulo-Erythematous Eruption and Neuritis of the Brachial Plexus After Injections of Penicillin. Eschboch, H.: Bull. et mém. Soc. méd. hôp. Paris **73**: 108, 1957.

An 85-year-old nonallergic man, who was in good health, was given five intramuscular injections of dideromycine bipenicillin during the course of a short febrile illness. Four days after his temperature had returned to normal, he developed an erythematous papular rash, a slight fever, and a lower radicular type of paralysis of the right brachial plexus. Within a fortnight the eruption cleared and there was some improvement in the extremity. After 6 months some weakness of the muscles remained. The author attributes these manifestations to the penicillin which the patient had received for the first time. I. G.

Anaphylaxis

Serotonin and Histamine Release During Anaphylaxis in the Rabbit. Waalkes, T. P., Weissbach, H., Bozicevich, J., and Udenfriend, S.: J. Clin. Invest. **36**: 1115, 1957.

Rabbits were sensitized to egg albumin or horse serum. Specific antigen was added to their blood samples in vitro. Free physiologically active serotonin and histamine values in samples so treated were 5 to 8 times greater than the values for control plasmas. The intravenous injection of specific

antigen in doses sufficient to produce rapid, labored breathing was associated with an immediate rise in both plasma histamine and plasma serotonin within one minute. The peak concentration of serotonin occurred about one minute after antigen injection and the histamine peak was reached at about 2 minutes. Levels of these substances then fell sharply, serotonin reaching a normal level at 4 to 5 minutes following antigen injection while histamine remained well elevated at this point. Although plasma serotonin and histamine were elevated, total circulating amines were markedly diminished due to the disappearance from the circulation of blood platelets and leukocytes which normally are rich in these substances. Minimum whole blood amine levels were reached in 4 minutes. Platelet counts became normal in from 1 to 2 hours, but the amine levels remained low for at least 4 hours, "suggesting that there had been a release of serotonin and histamine from the platelets." It is unknown whether serotonin is also released from other tissues known to contain it, such as lung, brain, and intestinal tract. The intravenous injection of serotonin and histamine in normal rabbits to produce plasma levels equivalent to those found in anaphylaxis required histamine doses of at least 50 gamma per kilogram and serotonin doses of about 150 gamma per kilogram. E. K.

Pharmacology, Physiology, and Pathology

Studies of Chemotaxis in a Simple Chamber Including Observations Using Cells From Allergic Human Subjects and Their Allergens. Smith, J. M.: J. Immunol. **77**: 133, 1956.

A technique for observing granulocyte migration and chemotactic activity within a chamber is described in detail. With this technique, permanent preparations may be prepared for the observation of phenomena occurring when various bacteria, solutions, or objects are placed in the path of the migrating cells.

The response of white blood cells obtained from 11 different subjects to a strain of *Staphylococcus aureus* was studied. On 4-hour-old preparations there was marked clumping of granulocytes which appeared to constitute a mechanical barrier to the bacteria. In 18-hour preparations, no free bacteria were visible within the migration zone of cells and many cells were full of bacteria and became round. Some of the bacteria-laden cells disintegrated and active climbing of granulocytes into the inoculation stab track was noted. At 24 hours, bacteria were seen emerging from some of the granulocytes. The response of the white cells from all subjects to the *S. aureus* was similar, regardless of whether the subjects showed positive or negative delayed cutaneous reactions to *S. aureus* vaccine. Similar consistent granulocytic responses were noted in preparations when a *Klebsiella pneumoniae* or a *Candida albicans* strain was employed. In experiments with the latter strain the responses were also similar, regardless of whether the subjects from which the white cells were obtained had positive or negative delayed skin reactions to *C. albicans* vaccine. When hemolytic streptococcus was employed chemotaxis, clumping, and climbing of granulocytes were absent and phagocytosis was irregular. With pneumococcus phagocytosis was also irregular, but chemotaxis, clumping, and climbing of granulocytes were marked in all preparations.

In another study white cells were obtained from 2 ragweed-sensitive patients and 2 nonsensitive persons. These cells were exposed to ragweed granules or to ragweed extract in the chamber. In all preparations there were no signs of chemotaxis, negative chemotaxis, or clumping of cells. The

granulocytes climbed along the fibers of the filter paper saturated with ragweed extract, but the same response was observed when the paper was saturated with buffered saline.

The finding that the activities of the granulocyte against a strain of bacteria or fungus are not affected by the presence of delayed skin reactivity to that organism is in accordance with the clinical observation that in sensitive persons there is no impairment of ability to localize infection with these organisms. B. S.

Pathology of Eosinophilic Granuloma of the Lung. Auld, D.: A. M. A. Arch. Path. **63**: 113, 1957.

The subject of eosinophilic granuloma of the lung is reviewed and three new cases are reported. The clinical aspects of this disease are described. It is noted that a mild eosinophilia of from 3 per cent to 10 per cent is found in about one-half the cases. The pathology is reported in detail. The lung lesions are in the form of granulomas in the interstitial tissue, and the essential cellular components are histiocytes and eosinophiles. A necrotizing arteriolitis with eosinophilic infiltration and fibrinoid degeneration of the arteriolar walls occurs. The lesions resemble those of periarteritis nodosa as well as those found in some cases of Loeffler's syndrome. Pathogenesis, etiology, and treatment are discussed.

It is suggested that eosinophilic granuloma of the lung may be a hypersensitivity reaction, probably due to an inhalant because of the diffuse pulmonary involvement, and that the condition may be a variation of Loeffler's syndrome. J. S.

Resynthesis of Adrenaline and Noradrenaline in the Adrenal Gland of the Cat. Butterworth, K. R., and Mann, M.: Nature **179**: 1079, 1957.

Atropinized cats were repeatedly injected intravenously with acetylcholine, thus depleting their adrenal glands of adrenaline and noradrenaline. One adrenal gland was removed as a control depleted gland and the animal was allowed to recover from the anesthetic. One month later the other gland was removed and its adrenaline and noradrenaline contents were determined biologically and chromatographically. There was an equal percentage increase in both amines, which had returned to their normal levels. In previous measurements done seven days after depletion, there had been a considerable increase in the level of noradrenaline, whereas the adrenaline had shown little resynthesis. The authors conclude that the rate of resynthesis of these amines in the cat's adrenal gland is slow and that adrenaline is synthesized from noradrenaline and not independently. I. G.

Pyribenzamine (Tripelennamine): Effects on Renal Hemodynamics and the Excretion of Water and Electrolytes. Moyer, J. H., Burgess, J., and Ford, R. V.: Am. Heart J. **54**: 643, 1957.

It has been reported that Pyribenzamine potentiates diuretic response to organic mercurials. Pyribenzamine in 25 or 50 mg. doses intravenously in dogs did not significantly alter urinary water and electrolyte excretion. Eighteen human subjects with mild heart failure and two adults with the nephrotic syndrome of glomerulonephritis were studied. Ten were given 50 mg. Pyribenzamine every 6 hours orally, 5 were given 50 mg. Pyribenzamine intravenously, 3 were given an organic mercurial concomitantly with Pyribenzamine, and the same 3 received the organic mercurial 48 or more hours

prior to an intramuscular injection of 50 mg. Pyribenzamine. The 2 nephrotic patients were given 25 mg. of Pyribenzamine intravenously. No significant changes were found in urinary sodium, potassium, or chloride. Neither were any significant changes found in inulin determinations of the glomerular filtration rate, para-aminohippurate determinations of the renal plasma flow, or in body weight. E. K.

Antihistaminic Protection Capacity of Cortisone and Its Derivatives (Experimental Study). Benda, R., Miravet, L. F., and Gartenlaub, G.: Bull. et mém. Soc. méd. hôp. Paris **73**: 284, 1957.

Twenty-eight guinea pigs with a natural resistance to aerosols of histamine of from 1.5 to 4 minutes were injected subcutaneously with cortisone, hydrocortisone, hemisuccinate of hydrocortisone, or hemisuccinate of delta-hydrocortisone. The antihistaminic protection capacity of these preparations, especially of hydrocortisone and cortisone, was demonstrated by a manifold increase in the histamine resistance time. The protective capacity reached a maximum 4 to 6 hours after the injection but lasted only a few hours.

I. G.

Immunology

The Influence of Adrenocorticotropic and Growth Hormones on Antibody Formation. Hayshida, T., and Li, C. H.: J. Exper. Med. **105**: 93, 1957.

A purified fraction of *Pasteurella pestis* was used as an antigen and injected intramuscularly into 3-month-old rats. ACTH was administered subcutaneously in doses sufficient to prevent growth for 5 days prior to and during the observation period. Serum antibody levels in rats treated in this manner were depressed (mean titer 1:21) as compared with controls (1:151).

The administration of the growth somatotropin (STH) alone failed to influence antibody production to a statistically significant degree at the 5 per cent level, although the animals gained weight rapidly. When STH was administered with ACTH the antibody depression produced by the latter was counteracted. It is suggested that antibody depression induced by ACTH is due to a decreased rate of protein synthesis. E. K.

Homologous Immunological Studies of Ocular Lens. I. In Vitro Observations. Halbert, S. P., Locatcher-Khorazo, D., Swick, L., Witmer, R., Seegal, B., and Fitzgerald, P.: J. Exper. Med. **105**: 439, 1957.

Adult rabbit eye lenses which were homogenized and incorporated in Freund's adjuvant mixture were injected into 5 groups of adult rabbits. One group of animals received rabbit lens in saline and one group received adjuvant mixture only. In another group rabbit lens in saline was injected into sites prepared 30 to 60 minutes earlier by the injection of streptolysin "O" concentrate, and additional controls received only streptolysin "O." Immunizing injections were given on 8 occasions over a one-year period, the first three injections being administered within a period of 15 days. The sites used were both flanks and the upper and lower back.

Antibody tests were done by the Ouchterlony agar diffusion technique, the hemagglutination technique with tanned red cells, and in a few instances by paper electrophoresis. Antibody could be detected in some animals at serum dilutions of 1:409,000. The hemagglutination technique was more sensitive than the agar precipitin method, precipitin bands never being found in sera which showed hemagglutination titers of less than 1:1600.

High levels of antibody resulted from administration of lens protein in Freund's adjuvant. Lens hemagglutination responses occurred in the animals immunized with homologous lens and streptolysin "O," although antibody response in this group was lower and was detected later than in the group treated with Freund's adjuvant and lens. Neither the animals given lens in saline nor any control animals developed detectable antibodies to lens protein. Early in the course of immunization only one precipitin band was seen in the agar. Later, 4 and even 5 precipitin bands appeared, particularly in sera with high hemagglutinin titers. There were no cross-reactions with rabbit brain, kidney, skin, liver, or plasma. Cross-reactions occurred with lenses of different species. The guinea pig and rat lenses showed 5 cross-reacting antigens with rabbit lens, and the mouse and frog lenses showed 4. Rooster lens gave 2 cross-reacting bands and fish (menhaden) lens one faint band. Cross-reactions occurred also with beef, rhesus monkey, and human lenses. Newborn rabbit and fetal rabbit lenses did not cross-react, although the electrophoretic pattern of these lenses is identical with that of adult rabbit lens. Cross-reaction is faint between 10-day-old rabbit lens and adult rabbit lens and is definite when 19-day-old rabbit lens is used. Lens dissection indicates that the adult lens antigen is mainly in the cortex of the lens. Photographs of the reaction bands on agar plates are presented. E. K.

Homologous Immunological Studies of Ocular Lens. II. Biological Aspects. Halbert, S. P., Locatcher-Khorazo, D., Swick, L., Witmer, R., Seegal, B., and Fitzgerald, P.: J. Exper. Med. **105**: 453, 1957.

Rabbits immunized to adult rabbit lens protein in Freund's adjuvant were examined by slit lamp for any lens abnormality. The aqueous humor was carefully removed and repeatedly assayed in 5 animals. The animals were bred and their offspring examined. No changes were found in either adult eyes or in the eyes of the offspring, despite the presence of high levels of circulating antibody to lens protein. Both the original aqueous humor and the humor reformed in animals subjected to the paracentesis procedure contained lens antibody in relatively low dilution. There were no detectable lesions of the lens or other ocular tissues. Matings of the experimental animals were much less fruitful than expected, even among animals receiving only Freund's adjuvant, and the maternal mortality rate among these animals was high for unknown reasons.

Sera taken from 200 human patients with cataracts were tested for antibody cataractous human lens protein by the agar diffusion technique. No antibodies were found, although in several sera a faint band appeared between the cataractous lens material and an adjacent serum well. It is suggested that this might represent a reaction to a component of human gamma globulin. E. K.

Impairment of the Antigenicity of a Protein Antigen Following Its Injection Into Rabbits. McMaster, P. D., and Edwards, J. L.: J. Exper. Med. **106**: 219, 1957.

Adult donor rabbits were injected intravenously with a single 100 mg. dose of bovine gamma globulin. Recipient rabbits were injected with a 5 mg. dose of bovine gamma globulin intravenously. When antigen disappeared from the circulation of the donors and when circulating antibody could not be detected in the recipients, homogenized liver tissue of the donors was injected intraperitoneally into the recipients. The liver tissue was frozen and stored prior to its injection into the recipients. Liver removed from animals 2 weeks

following immunization contained sufficient undegraded antigen to induce a recall antibody response in the recipient rabbits. When liver was taken 21 to 28 days after immunization of the donors, no such antibody response was obtained. It was determined that as little as 10 mcg. of bovine gamma globulin in saline intraperitoneally could elicit a recall antibody response in the recipient rabbits. Thus, the antigen was degraded after the second week to such an extent that it failed to engender the formation of complete antibody in the recipient animals. Previous work had shown that the transfer of liver tissue from similar donor rabbits to mice rendered the recipient mice anaphylactically sensitive to the antigen. E. K.

Production in Mice of Large Volumes of Ascites Fluid Containing Antibodies. Munoz, J.: Proc. Soc. Exper. Biol. & Med. **95**: 757, 1957.

Swiss-Webster female mice were used to produce ascites fluid containing antibodies. Each mouse received 2 injections of either bovine serum albumin (BSA) or 5 times recrystallized egg albumin mixed in Freund's adjuvant. The peritoneal cavity was tapped 2 weeks, 25 days, and 40 days after the last injection of the antigen-adjuvant mixture. The total amount of fluid collected from 8 mice in a period of 9 weeks was 143.5 ml., an average of 17.9 ml. of fluid per mouse. Two mice had insignificant amounts of fluid at the first tapping. Of 50 mice that received BSA, 38 (76 per cent) gave from 0.5 ml. to 13 ml. of fluid each. In another group of 50 animals receiving egg albumin, the number of mice giving significant amounts of fluid was somewhat smaller. Most of the fluids gave intense precipitation with egg albumin. A pool of the fluids from the first tapping was found to contain 213 mμ of antibody nitrogen per milliliter. As little as 0.05 ml. of peritoneal fluid containing 10 mμ of antibody nitrogen was sufficient to produce fatal passive anaphylaxis in pertussis-treated mice. The author points out that the above findings may be of great value in the investigations of mouse antibody as well as in the study of anaphylaxis with homologous antibody. The use of peritoneal fluid as a source of antibody would overcome the obstacle of limited amounts of serum obtainable from mice. T. CHAO.

Formation of Agglutinins to Shigella Paradysenteriae by Transfer of Lymph Node Cells. Harris, T. N., and Harris, S.: Federation Proc. **16**: 643, 1957.

Dysentery bacilli were injected into the hind feet of rabbits and the nodes were excised, 2, 3, and 4 days later or at shorter intervals. Cells obtained from the lymph nodes were washed and transferred to fresh recipients. Serum was obtained from the recipients at various intervals after transfer and tested for the presence of agglutinins to dysentery bacilli. When cells obtained 3 or 4 days after the injection of antigen into the donor were transferred to recipients, the agglutinins appeared on the first day after transfer. Generally the agglutinins reached maximum concentration by the third day and began to decline shortly thereafter. After the transfer of cells obtained at a 2-day interval, agglutinins appeared on the second day in the recipients; in the case of cells obtained at a 1-day interval, agglutinins appeared on the third day after transfer. In experiments involving donor intervals between 16 hours and 10 minutes, agglutinins were detected usually on the fourth day in the sera of irradiated recipients. These observations suggest that a period of approximately 3 days was required for the appearance of agglutinin as measured in this experiment and that this period of time could be divided between the donor and recipient rabbits. The studies were also performed with the lymph

node cell suspensions subjected to various injuries prior to transfer. The results indicated that viable cells were necessary for the antibody formation. In vitro studies using soluble forms of the antigen derived from *Shigella paradysenteriae*, cells from normal donor rabbits, and Shigella-treated antiserum gave evidence that an initial reaction between lymph node cells and antigen occurs within the first few minutes of the in vitro incubation. T. CHAO.

Miscellaneous

The Role of Vasoconstriction in the Local Shwartzman Reaction. Rall, D. P., and Kelly, M. G.: J. Exper. Med. **105**: 643, 1957.

The Shwartzman reaction was elicited in polysaccharide-prepared rabbits in the skin of the ear, the costovertebral angle, and the hind leg, in addition to the classic abdominal skin site, indicating a generalized skin preparatory state. Adrenolytic drugs, such as Dibenamine, reduced the percentage of positive Shwartzman reactions. Dihydroergotamine had no effect on the reaction, nor did two antihistamines. Vasoconstrictors, substituted for polysaccharide as the preparatory substance and administered intravenously, failed to act as preparatory agents. Epinephrine injected into the skin was, however, an effective preparatory agent. Heparin was administered to separate primary vasoconstriction from thrombosis. Reactions provoked by epinephrine in heparinized animals were more intense than in control animals. The adrenergic blocking drug SY-28 almost completely inhibited the reaction. Rabbits made leukopenic with nitrogen mustard were also more susceptible to epinephrine-induced Shwartzman reactions than were control animals. This report indicates "that peripheral vasoconstriction is involved in the Shwartzman phenomenon, and, indeed, may be a major factor in its development." E. K.

Strain Differences in Local Hemorrhagic Response (Shwartzman-Like Reaction) of Mice to a Single Intradermal Injection of Bacterial Polysaccharides. Kelly, M. G., Smith, N. H., Wodinsky, I., and Rall, D. P.: J. Exper. Med. **105**: 653, 1957.

Fourteen inbred strains of mice were examined for Shwartzman reactivity. Ten strains were found to be unreactive. In 3 strains and in one F hybrid subline a single intracutaneous injection of polysaccharide induced the typical lesion. The reaction differed from that in rabbits in that it appeared regardless of the usual provocative intravenous injection. The adrenergic blocking agent SY-28 and an anticoagulant, Coumadin, blocked the reaction in mice as they did in rabbits. E. K.

Attempted Passive Transfer of Thrombotic Thrombocytopenic Purpura. Brittingham, T. E., III., and Chaplin, H., Jr.: Blood **12**: 480, 1957.

A fatal case of idiopathic thrombotic thrombocytopenic purpura in a 35-year-old patient is described. The clinical findings consisted of purpura, hemolytic anemia, and neurological signs. On post-mortem examination, characteristic pathologic changes of thrombotic thrombocytopenic purpura were found. Laboratory tests had shown persistently low platelet counts, rapid bleeding time, markedly elevated reticulocyte counts, a mildly increased direct and indirect bilirubin, and a shortened red cell survival time. Bone marrow aspiration showed numerous megakaryocytes, erythroid hyperplasia, and normal white cell precursors. LE tests were negative. Neither leukoagglutinins nor platelet agglutinins could be demonstrated. The direct Coombs test was

also negative. The platelet count failed to change with large doses of ACTH, cortisone, and Meticorten. A splenectomy was performed on the twenty-seventh hospital day. The patient grew progressively worse and died 15 days later. A pint of the patient's blood drawn prior to therapy was citrated and centrifuged and 300 ml. of plasma was obtained. This was infused into a normal Group AB Rh-positive 32-year-old male volunteer. Frequent blood studies for the next 16 days revealed no significant changes. The recipient's temperature remained normal, and he developed no abnormal symptoms or blood findings for the next 10 months while he remained under observation. In view of all these facts, the authors believe "that antibodies against the formed elements of the blood were not significant in the pathogenesis of the patient's illness." R. W.

Announcement

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